Company Announcement

Results from Italfarmaco Pivotal Phase 3 EPIDYS Study of Givinostat in Duchenne Muscular Dystrophy (DMD) Published in *The Lancet Neurology*

Trial met primary endpoint: givinostat demonstrated statistically and clinically meaningful treatment benefit in one of the largest DMD phase 3 trials to date

Givinostat was well tolerated with a well-documented safety profile consistent with previous givinostat trials

Italfarmaco anticipates U.S. Food and Drug Administration (FDA) PDUFA response scheduled for March 21, 2024

MILAN, Italy, March 19, 2024 – Italfarmaco S.p.A. announced today that the full results from the Company's pivotal phase 3 EPIDYS clinical trial with givinostat in ambulant boys 6 years of age and older with Duchenne muscular dystrophy (DMD) have been published in *The Lancet Neurology*. The EPIDYS clinical trial met its primary endpoint: change in four-stair climb assessment from baseline to 72 weeks, which demonstrated the potential of givinostat to delay disease progression when added to corticosteroid treatment. Givinostat-treated boys also showed favorable outcomes on key secondary endpoints assessed in the study. The full manuscript, titled, "Safety and efficacy of givinostat in boys with Duchenne muscular dystrophy (EPIDYS): a multicentre, randomized, double-blind, placebo-controlled, phase 3 trial," is published on The Lancet Neurology website.

"DMD is an unforgiving degenerative disease with significant unmet medical need and givinostat has the potential, if approved, to benefit a broad DMD patient population independent of the underlying gene mutation," said **Eugenio Mercuri, MD, Professor of Paediatric Neurology at the Catholic University, Rome, Italy.** "The givinostat-treated group fared better than the control group in a range of muscle function and strength tests at 72 weeks."

"When managing DMD, a primary goal is to maintain motor function for as long as possible. The results from EPIDYS provide robust evidence that givinostat has the potential to support this goal," added **Craig M. McDonald, MD, Professor at the Department of Pediatrics and Physical Medicine Rehabilitation at the University of California Davis Health.** "In addition to the primary endpoint, analysis of the North Star Ambulatory Assessment (NSAA), which measures motor function skills based on a 17-item rating scale, showed that treatment with givinostat resulted in 40% less decline compared to the control group. Taken together, these data suggest givinostat could be an effective new treatment for DMD management."

"The results of the phase 3 EPIDYS study are encouraging and highlight the dedication of Italfarmaco's research and clinical teams to achieve this milestone for the company," said **Paolo Bettica, MD, PhD, Chief Medical Officer at Italfarmaco Group**. "We want to thank all the individuals and their families who participated in this international study and would also like to acknowledge the tireless efforts of the clinical investigators as well as the unwavering support of the DMD community."

Overview of Phase 3 EPIDYS Clinical Trial

EPIDYS was a multicentre, randomised, double-blind, placebo-controlled phase 3 trial which enrolled 179 ambulant boys 6 years of age or older with DMD across clinical sites in North

America and Europe (NCT02851797). Participants were randomised 2:1 to receive oral givinostat or matching placebo twice daily along with their corticosteroid treatment regimen. Participants attended study site visits every 12 weeks for 72 weeks and were evaluated for all endpoints within the study protocol.

Key clinical findings supporting the potential of givinostat in improving clinical outcomes in DMD:

Primary endpoint: The study met its primary endpoint, which measured the mean change between baseline and 72 weeks in the ability to climb four stairs. Participants that received givinostat demonstrated a slower decline in performing this functional task compared to the placebo group (difference vs. placebo of 1.78 seconds, p=0.037).

Key secondary endpoints: A number of secondary endpoints that evaluated muscle function and strength showed favourable results in the givinostat-treated cohort compared to the control group. In particular, givinostat treatment was associated with 40% less decline in NSAA total score and item loss, indicating givinostat's potential to delay disease progression in affected individuals. The EPIDYS study also evaluated fat infiltration in the vastus lateralis (VL) muscle of the thigh by magnetic resonance imaging. The vastus lateralis fat fraction (VLFF) is a predictor of loss of ambulation and indicates disease progression in DMD individuals. Givinostat-treated individuals had a 30% reduction in VLFF compared to the placebo-treated cohort. Overall, the analyses of the secondary endpoints showed delayed disease progression with givinostat treatment.

Safety and tolerability: During the study, the most common treatment-related adverse events (frequency ≥1/10 boys) associated with givinostat were decreased platelet count/thrombocytopenia, increased blood triglyceride/hypertriglyceridemia, diarrhoea and abdominal pain; none of the severe or serious adverse events were treatment-related or resulted in study withdrawal. Givinostat tolerability was managed with appropriate monitoring and dose adjustments. No other safety concerns were observed.

Open-label Extension Clinical Study (OLE study)

Upon completion of the 18-month double-blind period, EPIDYS study participants were eligible to enroll in an open-label extension study (OLE study) to receive givinostat on an ongoing basis. The median follow up of participants in the EPIDYS + OLE studies is 4.7 years.

Givinostat received priority review, orphan drug and rare pediatric disease designations from the FDA and orphan drug designation from the European Commission. A New Drug Application (NDA) was filed with the U.S. FDA and the Prescription Drug User Free Act (PDUFA) date for givinostat is March 21, 2024. A Marketing Authorisation Application (MAA) for givinostat has been submitted to the European Medicines Agency (EMA) and is currently under review.

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a severe neuromuscular genetic disease characterised by progressive muscle weakness and degeneration and is the most common type of muscular dystrophy globally. DMD is caused by mutations in the dystrophin gene that result in the absence of a functional dystrophin protein. Without dystrophin, muscle fibres are highly susceptible to injury and this continuous muscle injury leads to chronic inflammation, impairment of muscle regeneration and muscle replacement by fibrotic and fat tissue. The disease primarily affects boys, with symptoms usually first seen between two and five years of age. Symptoms worsen over time affecting the ability to walk. Eventually, heart and

respiratory muscles are affected, which are the two main causes of premature death. DMD incidence is approximately one in every 3500 - 6000 male births worldwide.

About Givinostat

Givinostat is an investigational drug discovered through Italfarmaco Group's research and development efforts in collaboration with Telethon and Duchenne Parent Project (Italy). Givinostat is a histone deacetylase (HDAC) inhibitor that modulates the deregulated activity of HDACs in the dystrophic muscle, which is a major consequence of the lack of dystrophin associated with DMD. Givinostat's mechanism of action has the potential to inhibit HDAC pathological overactivity in an effort to address the cascade of events leading to muscle damage, thereby counteracting the disease pathology and slowing down muscle deterioration.

About ITALFARMACO

Founded in 1938 in Milan, Italy, Italfarmaco S.p.A. is a private global pharmaceutical company that has led the successful development and approval of many pharmaceutical products around the world. Italfarmaco S.p.A. has operations in more than 60 countries through directly controlled or affiliated companies. The company is a leader in pharmaceutical research, product development, production and commercialisation with proven success in many therapeutic areas including immuno-oncology, gynaecology, neurology, cardiovascular disease and rare diseases. Italfarmaco's rare disease unit includes programmes in Duchenne muscular dystrophy, Becker muscular dystrophy, amyotrophic lateral sclerosis and polycythaemia vera.

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